AMENDMENTS

In the Claims

108. (Amended) An aerosolizable or sprayable [pharmaceutical] composition, comprising a carrier, a nucleic acid [in the form of an aerosol] that comprises one or more oligonuceleotide(s) (oligo(s)) effective to alleviate hyper-responsiveness to [, and/or increased levels of,] adenosine, bronchoconstriction, asthma, lung allergy[(ies)] [and/or] lung inflammation, or to reduce levels of adenosine receptor(s) [and contains up to and including about 15% adenosine (A),] ; wherein the oligo [being] is anti-sense to an initiation codon, a coding region or a 5' or 3' intron-exon junction [s] of a gene[(s)] encoding an adenosine A_1, A_{2a}, A_{2b}, or A_3 receptor or is anti-sense to their corresponding [respective] mRNA(s), [;] pharmaceutically and veterinarily acceptable salts of the oligo(s) or mixtures thereof [, and a surfactant that may be operatively linked to the nucleic acid].

109. (Amended) The composition of claim 108, wherein the oligo [consists of] comprises up to about 10%A.

110. (Amended) The composition of claim 109, wherein the oligo [consists of] comprises up to about 5%A.

111. (Amended) The composition of claim 110, wherein the oligo [consists of] comprises up to about 3%A.

112. (Reiterated) The composition of claim 111, wherein the oligo is A-free.

113. (Amended) The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3'intron-exon junctions or to sequences of the coding region comprising 2 or more G [and/]or C of the adenosine A_1 receptor gene.

114. (Amended) The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3'intron-exon junctions or to sequences of the coding region comprising 2 or more G [and/]or C of the adenosine A_{2a}, A_{2b} [and/]or A_3

receptors.

115. (Amended) The composition of claim 108, wherein if the oligo contains adenosine (A), at least one A is substituted by a [universal base selected from the group consisting of] heteroaromatic base[s] that binds to a thymidine base but [have] has antagonist activity [and] or has less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b}, [and] or A_3 receptors, [and] or heteroaromatic base[s] that [have] has no activity or [have] has agonist activity at the adenosine A_{2a} receptor.

116. (Amended) The composition of claim 115, wherein substantially all As are substituted by a [universal base(s) selected from] heteroaromatic base[s] that binds to a thymidine base but [either have] has antagonist activity or has less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} [and] or A_3 receptors, [and] or heteroaromatic base[s] that [have] has no activity or [have] has agonist activity at the adenosine A_{2a} receptor.

117. (Amended) The composition of claim 115, wherein the heteroaromatic base[s are] is selected from a pyrimidine[s] or purine[s that may be] substituted by an O, halo, NH_2, SH, SO, SO_2, SO_3, COOH, or branched or fused primary or secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalhl, arylalkenyl, arylalkynyl, or arylcycloalkl [, which may be further substituted b O, halo, NH_2, primary, secondary or tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl].

118. (Amended) The composition of claim 117, wherein the pyrimidines are substituted at a 1, 2, 3, [and/]or 4 position, and the purines are substituted at a 1, 2, 3, 4, 6, 7 [and/]or 8 position.

119. (Amended) The composition of claim 118, wherein the pyrimidines or purines are one selected from theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline [or xantine] and xanthine.

120. (Amended) The composition of claim 116, wherein the universal base is one selected from 3 nitropyrrole-2 '-deoxynucleoside, 5-nitroindole, 2-deoxyribosyl (5-nitroindole), 2-deoxyribofuranosyl (5 -nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H 8H-3, 4-dihydropyrimido [4, 5 -c] oxazine -7 -one [or] and 2 -amino -6 -methoxyaminopurine.

121. (Amended) The composition of claim 108, wherein said nucleic acid comprises a methylated cytosine [(^{m}C) is substituted for an unmethylated cytosine (C) in at least one CpG dinucleotide if present in the nucleic acid(s)] adjacent 5' to a guanosine.

122. (Amended) The composition of claim 108, wherein at least one monoculeotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether,carbonate, 5'-N-carbamate sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) [and] , methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl-pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2 'propoxy, C-N3 18'- amine, PS phosphoramidates, 3'-alkylamino,2 '-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-0-(2-methoxy) ethyl, 2'-0-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone [sulfatide] (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly I -lysine, sulfatidic acid or a fatty acid[s].

123. (Amended) The composition of claim 122, wherein substantially all mononucleotides are linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether,carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) [and] , methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol,

terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy,C-18 amine, N3'-P5 ' phosphoramidates, 3 '-alkylamino, 2 '-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2 '-borano, C-5 hexynyl pyrimidine, 2'-O-aminopropyl,5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugatd to a polyethylene, glycol, cholestrol, cholesteryl , dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid[s].

124. (Amended) The composition of claim 108, wherein the anti-sense oligo comprises [about] 7 to 60 mononucleotides.

125. (Amended) The composition of claim 108, wherein the oligo comprises a sequence selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 [or DEC] and SEQ ID NO: 7 to SEQ ID NO: 966, or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 [or] and SEQ ID NO: 7 to SEQ ID NO: 966, wherein at least one mononucleotide is linked or modified by one or more of [phoshporothioate] phosphorothioate , phosphorodithioate, phosphorotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether,carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) [and] , methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or a peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA Sulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid[s].

126. (Amended) The composition of claim 108, wherein the nucleic acid is linked to an agent that enhances cell internalization or up-take [and/]or a cell targeting agent.

127. (Amended) The composition of claim 126, wherein the cell internalization or uptake enhancing agent is a transferrin, [a]sialoglycoprotein or [a] streptavidin.

128. (Reiterated) The composition of claim 126, wherein the cell targeting agent comprises a vector, and the nucleic acid is operatively linked to the vector.

129. (Reiterated) The composition of claim 128, wherein the vector comprises a prokaryotic or eukaryotic vector.

130. (Amended) The composition of claim 108, wherein the surfactant comprises a surfactant protein, phospholipid, fatty acid, or surfactant-associated protein, or mixtures thereof [is selected from surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein D or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters, phosphatidyl ethers, palmitates, tyloxapol, phospholipids, fatty acids, surfactant-associated proteins or $C_{22}H_{19}C_{10}$].

131. (Amended) The composition of claim 130, wherein the surfactant [is selected from] comprises a polyoxy ethylene 23 lauryl ether (Brij 35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC®), tyloxapol (Exosurf®), phospholipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}[C_{10}]ClO_3$ (Atovaquone®).

132. (Reiterated) The composition of claim 108, wherein the carrier comprises a biologically acceptable carrier.

134. (Reiterated) The composition of claim 108, wherein the carrier is a pharmaceutically or veterinarily acceptable carrier.

135. (Amended) The composition of claim 134, wherein the carrier is [selected from gaseous,] a liquid or solid carrier[s].

136. (Amended) The composition of claim 108, further comprising an agent [selected from] wherein said agent is a therapeutic agent[s other than the nucleic acid(s)], antioxidant[s], [flavoring or] coloring agent[s], filler[s], volatile oil[s], buffering agent[s], dispersant[s], RNA inactivating agent[s], flavoring agent[s], propellant[s] or preservative[s].

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137. (Amended) The composition of claim 136, [comprising] wherein said carrier is a pharmaceutically or veterinarily acceptable carrier [, the nucleic acid, a surfactant, and other said therapeutic agents].

138. (Reiterated) The composition of claim 136, wherein the RNA inactivating agent comprises an enzyme.

139. (Reiterated) The composition of claim 138, wherein the enzyme comprises a ribozyme.

140. (Reiterated) The composition of claim 108, further comprising a propellant.

141. (Reiterated) The composition of claim 108, wherein the nucleic acid is present in an amount of about 0.01 to about 99.99 w/w of the composition.

143. (Amended) The [formulation] composition of claim 108, wherein said composition is a [selected from] intrabuccal, intrapulmonary, respirable, nasal, inhalable, intracavitary, intraorgan, or slow release formulation[s].

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144. (Amended) The [formulation] composition of claim 143, wherein the carrier is [selected from] a gaseous propellant , or solid or liquid carrier.

146. (Amended) The [aerosol or spray formulation] composition of claim 108, [which] wherein said composition is [selected from] a powder[s, sprays], solution[s], suspension[s] or emulsion[s].

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148. (Amended) The [aerosol or spray formulation] composition of claim 108,

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which is [selected from] an aqueous [or] solution, alcoholic solution[s or] aqueous suspension, alcoholic suspension[s], oily solution[s or] , oily suspension[s], [or] oil-in-water emulsion or water-in-oil emulsion[s].

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151. (Amended) A capsule or cartridge, comprising the [formulation] composition of claim 143.

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152. (Amended) The [spray or aerosol formulation] composition of claim 146, comprising a sprayable or aerosolizable solid powder [ed spray or aerosol].

153. (Amended) The [formulation] composition of claim 108, wherein the carrier comprises a hydrophobic carrier.

158. (Amended) The [formulation] composition of claim 143, which comprises an intrapulmonary, intracavitary or intraorgan liquid or solid powdered formulation of particle size about 0.5μ to about 10μ, or [about] 10μ to [about] 500μ.

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159. (Amended) The [formulation] composition of claim 143, which comprises a nasal formulation of particle size [about] 10μ to [about] 500μ.

161. (Amended) The [formulation] composition of claim 143, in bulk, or in single or multiple unit dose form.

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162. (Amended) The [formulation] composition of claim 143, which is a respirable or inhalable formulation comprising a solid powdered or liquid aerosol or spray of particle size about 0.5μ to about 10μ.

163. (Reiterated) A single cell, comprising the nucleic acid of claim 108.

164. (Amended) A diagnostic or therapeutic kit for delivery of an oligonucleotide(s) (oligo(s)) [diagnosis or treatment of diseases and conditions associated with hypersensitivity or and/or increased levels of, adenosine and/or adenosine receptor(s) and/or bronchoconstriction and/or lung allergy(ies) and/or lung inflammation and/or asthma] comprising, in separate containers,

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the delivery device of claim 222;

a nucleic acid comprising at least one oligonucleotide (oligo) [effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, to alleviate bronchoconstriction, asthma lung allergy(ies)and/or lung inflammation, the oligo being anti-sense to the initiation codon, the coding region or the 5'or 3 ' intron-exon junctions of a gene encoding a protein associated with hyper responsiveness to, and/or increased levels of, adenosine, with bronchoconstriction, asthma, lung allergy(ies)lung inflammation, or being anti-sense to the corresponding mRNA; the nucleic acid comprising one or more oligo(s)], their mixtures or their pharmaceutically or veterinarily acceptable salts; and

instructions for preparation of a non-liposomal respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation[s] of the nucleic acid of particle size about 0.5 to [about] 500μ for its use [; and

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optionally an agent selected from therapeutic or diagnostic agents other than the oligo(s), anti-oxidants, fillers, volatile oils, dispersants, anti-oxidants, flavoring agents, propellants, preservatives, solvents, surfactants, buffering agents, RNA inactivating agents, agents that are internalized or up-taken by a cell, or coloring agents] .

165. (Amended) The kit of claim 164, wherein the delivery device [comprises a nebulizer that] delivers single metered doses of a solid powdered or liquid aerosol or spray inhalable, respirable, intracavitary, intraorgan or intrapulmonary formulation of the nucleic acid of particle size about 0.5μ to about 10μ or [about] 10μ to [about] 500μ [of the nucleic acid].

166. (Amended) The kit of claim 164, wherein the device [comprises an insufflator] is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray; and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as a non-liposomal nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of the nucleic acid of particle size about 0.5μ to about 10μ or [about] 10μ to [about] 500μ.

167. (Amended) The kit of claim 164, wherein the delivery device comprises a

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pressurized [inhaler] device that delivers a solid powdered or liquid aerosol or spray of particle size about 0.5μ to about 10μ or [about] 10μ to [about] 500μ; and the nucleic acid is provided as a non-liposomal suspension, solution, emulsion or dry powdered aerosolizable or sprayable formulation of about 0.5μ to about 10μ or [about] 10μ to [about] 500μ.

Cancel Claim 168.

169. (Amended) The kit of claim 164, wherein the solvent is [selected from] an organic solvent[s] or an organic solvent[s] mixed with one or more co-solvents.

170. (Amended) The kit of claim 164, wherein the device is adapted for receiving a capsule(s) or cartridge(s), and the nucleic acid is [separately] provided as a non-liposomal inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation in a capsule(s) or cartridge(s).

171. (Amended) The kit of claim 164 further comprising, in separate containers, a propellant, [and] a pressurized means for delivery adapted for delivering a solid powdered or liquid aerosol or spray, and instructions for loading into the delivery device the nucleic acid as an inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation of particle size about 0.5 μ to about 10μ or [about] 10μ to [about] 500 μ, and then joining the device with the propellant and the pressurized means.

172. (Reiterated) The kit of claim 167, wherein the pressurized inhaler further comprises a propellant and means for delivery of the propellant, and delivers the nucleic acid as a liquid or solid powdered aerosol or spray formulation.

173. (Amended) An in vivo method of delivering a pharmaceutical composition to a target polynucleotide(s) comprising administering to the airways of a subject an aerosol or spray non-liposomal composition of particle size about 0.5 μ to about 10 μ or [about] 10 μ to [about] 500 μ comprising a nucleic acid(s) that comprises at least one oligonucleotide(s) (oligo(s)) [effective to alleviate hyper-responsiveness to, and/or increased levels of adenosine, or to alleviate bronchoconstriction, and/or asthma and/or lung allergy(ies) and/or lung

inflammation, the oligo containing up to and including about 15% adenosine (*A*), and being anti-sense to the initiation codon, the coding region or the 5' or 3 'intron-exon junctions of a gene encoding a protein associated with hyper responsiveness to, and/or increased levels of, adenosine, bronchoconstriction, asthma and/or lung allergy(ies), and/or lung inflammation, or being anti-sense to the corresponding mRNA].

178. (Amended) The method of claim 173, wherein the composition is administered [intrapulmonary, intraorgan, intracavitarily, intrabuccally, intranasally,] by inhalation [or] into the subject's respiratory system.

179. (Amended) The method of claim 173, wherein the oligo(s) is(are) anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene encoding a protein associated with hyper-responsiveness to adenosine, increased levels of adenosine, increased levels of an adenosine receptor, bronchoconsriction, asthma, lung allergy or lung inflammation, or is anti-sense to the corresponding mRNA, and is(are) effective to reduce hyper-responsiveness to adenosine, [and/or] to reduce the amount of adenosine receptor(s) [and/or] , to reduce the production or availability of adenosine, [and/] or to increase the degradation of mRNA encoding the adenosine receptor [mRNA(s)].

180. (Amended) The method of claim 178, wherein the oligo(s) is(are) administered directly into the subject[;]'s lung(s), intraorgan, intracavitarily, intrabuccal or intrapulmonarily.

181. (Amended) The method of claim [178] 173, wherein the composition comprises solid powdered or liquid particles of the nucleic acid(s) about 0.5 to about 10 μ in size.

183. (Amended) The method of claim [181] 173, wherein the composition is administered as powdered solid or liquid nucleic acid particles [greater than about] 10 μ to 500 μ in size.

184. (Amended) The method of claim 173, wherein the non-liposomal composition further comprises a surfactant.

185. (Amended) The method of claim [173] 179, wherein the hyper-responsiveness to [and/or] adenosine, increased levels of [,] adenosine , increased levels of an adenosine

receptor, asthma [or] , lung allergy[(ies)] or lung inflammation is associated with bronchoconstriction [,] of lung airways.

186. (Amended) The method of claim 185, wherein the hyper-responsiveness to adenosine, [or] increased levels of [,] adenosine, increased levels of an adenosine receptor, bronchoconstriction, [or] lung allergy[(ies)] or lung inflammation is[(are)] associated with allergies, COPD, asthma, ARDS, RDS, CF or side effects of adenosine administration.

187. (Amended) The method of claim [173] 179, wherein the hyper-responsiveness to adenosine , [or] increased levels of [,] adenosine, increased levels of an adenosine receptor, bronchoconstriction, asthma, lung allergy[(ies) and/]or lung inflammation is[(are)] associated with inflammation or an inflammatory disease.

188. (Reiterated) The method of claim 173, wherein the composition further comprises other therapeutic agents.

189. (Amended) The method of claim 188, wherein the other therapeutic agents comprise anti-adenosine A_1, A_{2b} or A_3 receptor agents or adenosine A_{2a} receptor stimulating agents other than the nucleic acid(s).

191. (Amended) The method of claim [190] 184, wherein the surfactant comprises a surfactant protein, non-liposomal phospholipid, fatty acid or surfactant-associated protein, or a mixture thereof [surfactant protein A, surfactant protein B, surfactant protein C surfactant protein D or active fragments thereof, non-dipalmitoyl disaturated phosphatidycholine, dipalmitoylphosphatidylcholine, phosphatidycholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy

alcohols, phosphatidyl choline esters, phosphatidyl ethers, palmitates, tyloxapol, phospholipids, fatty acids, surfactant-associated proteins or $C_{22}H_{10}C_{10}$].

192. (Reiterated) The method of claim 173, wherein the subject is a mammal.

193. (Amended) The method of claim 192, wherein the mammal is a human [or a non-human mammal].

195. (Amended) The method of claim 173, wherein the nucleic acid is administered in an amount of about 0.005 to about 150 mg/kg body weight.

196. (Reiterated) The method of claim 195, wherein the nucleic acid is administered in an amount of about 0.01 to about 75 mg/kg body weight.

197. (Reiterated) The method of claim 196, wherein the nucleic acid is administered in an amount of about 1 to about 50 mg/kg body weight.

198. (Amended) The method of claim 173, [which] wherein said method is a prophylactic or therapeutic method.

200. (Amended) The method of claim [173] 179, wherein the nucleic acid is obtained by

(a) selecting fragments of a target nucleic acid having at least 4 contiguous bases consisting of G or C; and,

(b) obtaining a second oligo 4 to 60 nucleotides long comprising a sequence that is anti-sense to the selected fragment

[, the second oligo having an A base content of up to and including about 15%].

201. (Amended) The method of claim 173, wherein the oligo [consists of] comprises up to about 10% A.

202. (Amended) The method of claim 201, wherein the oligo [consists of] comprises up to about 5% A.

203. (Amended) The method of claim 20 1, wherein the oligo [consists of] comprises

alcohols, phosphatidyl choline esters, phosphatidyl ethers, palmitates, tyloxapol, phospholipids, fatty acids, surfactant-associated proteins or $C_{22}H_{10}C_{10}$].

192. (Reiterated) The method of claim 173, wherein the subject is a mammal.

193. (Amended) The method of claim 192, wherein the mammal is a human [or a non-human mammal].

195. (Amended) The method of claim 173, wherein the nucleic acid is administered in an amount of about 0.005 to about 150 mg/kg body weight.

196. (Reiterated) The method of claim 195, wherein the nucleic acid is administered in an amount of about 0.01 to about 75 mg/kg body weight.

197. (Reiterated) The method of claim 196, wherein the nucleic acid is administered in an amount of about 1 to about 50 mg/kg body weight.

198. (Amended) The method of claim 173, [which] wherein said method is a prophylactic or therapeutic method.

200. (Amended) The method of claim [173] 179, wherein the nucleic acid is obtained by

(a) selecting fragments of a target nucleic acid having at least 4 contiguous bases consisting of G or C; and,

(b) obtaining a second oligo 4 to 60 nucleotides long comprising a sequence that is anti-sense to the selected fragment

[, the second oligo having an A base content of up to and including about 15%].

201. (Amended) The method of claim 173, wherein the oligo [consists of] comprises up to about 10% A.

202. (Amended) The method of claim 201, wherein the oligo [consists of] comprises up to about 5% A.

203. (Amended) The method of claim 20 1, wherein the oligo [consists of] comprises

up to about 3% A.

204. (Reiterated) The method of claim 203, wherein the oligo is A-free.

205. (Amended) The method of claim [173] 179, wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding an adenosine A_1, A_{2b} or A_3 receptor, and the composition further comprise[s] a surfactant.

206. (Amended) The method of claim 173, wherein if the oligo contains A, wherein at least one said A is substituted with a [universal base selected from] heteroaromatic base[s] which binds to a thymidine base but [have] has an antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b}, or A_3 receptors, or a heteroaromatic base[s] which [have] has no activity or [have] has agonist activity at the adenosine A_{2a} receptor.

207. (Amended) The method of claim 206, wherein substantially all As are each substituted with [universal bases selected from] a heteroaromatic base[s] which binds to a thymidine base but [have] has an antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b}, or A_3 receptors, or a heteroaromatic base[s] which [have] has no activity or [have] has agonist activity at the adenosine A_{2a} receptor.

208. (Amended) The method of claim 206, wherein the heteroaromatic base[s are selected from] is a pyrimidine[s] or purine[s that may be] substituted by an O, halo, NH_2, SH, SO, SO_2, SO_3, COOH, branched fused primary secondary amino, alkyl, alkenyl alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, or arylcycloalkyl [, all of which may be further substituted by O, halo, NH_2, primary, secondary and tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl].

209. (Amended) The method of claim 208, wherein the pyrimidine[s are] is substituted at position[s] 1, 2, 3 [and/]or 4, and the purine[s are] is substituted at position[s] 1, 2, 3, 4, 6, 7 [and/]or 8.

210. (Amended) The method of claim 209, wherein the pyrimidine [s] and purine[s are selected from] is theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xanthine [xantine].

211. (Amended) The method of claim 206, wherein the [universal] heteroaromatic base comprises 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido [4,5-c] oxazine-7-one or 2-amino-6-methodxyaminopurine.

212. (Amended) The method of claim 173, [further comprising methylating at least one] wherein said oligonucleotide comprises a methylated cytosine vicinal to a guanosine [into a methylated cytosine (^{m}C) if a CpG dinucleotide is present in the oligo(s)].

213. (Reiterated) The method of claim 173, further comprising modifying or substituting at least one mononucleotide of the anti-sense oligo(s) with methylphosphonate, phosphotriester, phosphorothioate, phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene(methyimino), methyleneoxy (methylimino), 2'-O-methyl, phosphoramidate residues, or combinations thereof.

214. (Amended) The method of claim 213, wherein substantially all mononucleotides are substituted [and/]or modified.

215. (Amended) The method of claim 173, [further comprising operatively linking] the nucleic acid is operatively linked to an agent that enhances cell internalization or up-take, or a cell targeting agent.

216. (Amended) The method of claim 215, wherein the agent that enhances cell internalization or up-take [enhancing agent] is [selected from] transferrin, asialoglycoprotein or streptavidin.

217. (Reiterated) The method of claim 215, wherein the cell targeting agent comprises a vector.

218. (Amended) The method of claim 217, wherein the vector [to which the agent] is [operatively linked] comprises a prokaryotic or eukaryotic vector.

219. (Amended) The method of claim [173] 179, wherein the nucleic acid comprises an oligo of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO:[998] 966, or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO:[998] 966, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether,carbonate 5'-N-carbamate,sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-0-methoxyethyl,C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2' propoxy, C-18 amine, N3'-P5 phosphoramidates, 3 '-alkylamino, 2 '-fluoro [;] pyrimidine, 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxyethyl, 2'-0-aminopropyl, 5-(phenylethyl) or a peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone [sulfatide] (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid[s].

220. (Amended) The method of claim 191, wherein the surfactant is [selected from] polyoxy ethylene 23 lauryl ether (Brij35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC ®), (Exosurf®), phospholipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}[C_{10}]ClO_3$ (Atovaquone®).

221. (Amended) The method of claim [173] 179, wherein the hyper-responsiveness to adenosine, [or] increased levels of[,] adenosine, increased levels of an adenosine receptor, bronchoconstriction, lung allergy[(ies)] or lung inflammation, is associated with asthma or a disease or condition associated with asthma.

222. (Amended) A diagnostic or therapeutic device adapted for delivering a non-

liposomal respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation of particle size about 0.5 μ to [about] 500 μ, wherein the formulation [comprising] comprises a nucleic acid(s) [that comprise] comprising at least one oligonucleotide (oligo(s)), or mixture thereof, or pharmaceutically or veterinarily acceptable salts thereof, [effective for diagnosing or treating hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, asthma, or lung allergy(ies) or lung inflammation, or a disease or condition associated with either of them, the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, asthma, or lung allergy(ies) or lung inflammation, or being anti-sense to the corresponding mRNA(s); the nucleic acid(s) comprising one or more oligo(s), their mixtures, or their pharmaceutically or veterinarily acceptable salts.]

223. (Amended) The device of claim 222, [comprising a nebulizer] wherein said device is adapted for delivering single metered doses of the formulation as a solid powdered or liquid aerosol or spray of the nucleic acid of particle size about 0.5μ to about 10 μ or [about] 10 μ to [about] 500 μ.

224. (Amended) The device of claim 222, [which comprises an insufflator] wherein said device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s), and for producing a solid powdered or liquid aerosol or spray of particle size about 0.5 μ to about 10 μ or [about] 10 μ to [about] 500 μ and wherein the formulation is provided separately in [a piercable or openable] said capsule(s) or cartridge(s) as a nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of particle size about 0.5 μ to about 10 μ or [about] 10 μ to [about] 500 μ.

225. (Amended) The device of claim 222, [which comprises a pressurized inhaler that] wherein said device is pressurized and delivers a solid powdered or liquid aerosol or spray formulation of particle size about 0.5 μ to about 10 μ or, or [about] 10 μ to [about] 500 μ; wherein the formulation comprises a suspension, solution, emulsion or dry powder aerosol or spray of the nucleic acid.

226. (Amended) The [pressurized inhaler] device of claim 225, further comprising, in

separate containers [,] ; a propellant and [pressurized] means for [delivery adapted for] delivering a solid powdered or liquid aerosol or spray, and instructions for loading into the [delivery] device the [inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary] formulation [,] and joining the device with the propellant and the pressurized [delivery] means for delivery

227. (Amended) The [pressurized inhaler] device of claim 225, further comprising a propellant and [propellant delivery] means for delivering [, wherein the pressurized inhaler delivers] the formulation as a liquid or solid powdered aerosol or spray.

228. (Amended) The device of claim 222, [which] wherein said device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s), and wherein the formulation is provided separately in [a] the capsule(s) or cartridge(s).

229. (Amended) The kit of claim 164, wherein the oligo(s) is (are) anti-sense to the initiation codon, the coding region or the 5' or 3' region of a gene encoding a polypeptide [selected from] wherein said polypeptide is an adenosine A_1 receptor, adenosine A_{2a} receptor, adenosine A_{2b} receptor, or adenosine A_3 receptor.

230. (Reiterated) The kit of claim 229, for diagnosis or treatment of sepsis, pulmonary vasoconstriction, lung inflammation, or lung allergies, asthma, impeded respiration, respiratory distress syndrome (RDS), acute respiratory distress syndrome (ARDS), pain, cystic fibrosis (CF), pulmonary hypertension, pulmonary vasoconstriction, emphysema or chronic obstructive pulmonary disease (COPD).

231. (Amended) The kit of claim 164, wherein the nucleic acid comprises an oligo of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'N carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) [and] , methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2 'propoxy,

C-18 amine, N3'-P5 phosphoramidates, 3 '-alkylamino, 2'-fluoro [;] pyrimidine, 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-0-(2-methoxy)ethyl, 2'-0-aminopropyl, 5-(phenylethyl) or a peptide nucleic acid inter base linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone [sulfatide] (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid[s].

232. (Amended) The composition of claim 108, [which] wherein, upon aerolization and spraying, said composition comprises particle sizes of about 0.5 μ to about 10 μ or [about] 10 μ to [about] 500 μ.

233. (Reiterated) The nucleic acid of claim 108, which is operatively linked to a vector.

234. (Amended) A [single] cell [,] comprising the nucleic acid of claim 233.

Please add the following claims:

--235. (New) The composition of claim 108, wherein the oligo(s) comprises up to about 15% A.

236. (New) The composition of claim 130, wherein the surfactant is selected from the group consisting of surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E, or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate diacylglycerol, cytidine diphosphate choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acid, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene oxide block copolymers, non-ionic propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran side chains, poly (vinyl amine) with alkanoyl side chains, polyoxy ethylene

ether, phenoxy polyethoxy alcohol, phosphatidyl choline ester, phosphatidyl ether, tyloxapol, and $C_{22}H_{19}ClO_3$.

237. (New) The kit of claim 164, wherein the surfactant is selected from the group consisting of surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E, or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate diacylglycerol, cytidine diphosphate choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acid, polyenic acid, polyenoic acid, lecithin, pahnitic acid, non-ionic ethylene oxide block copolymers, non-ionic propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran side chains, poly (vinyl amine) with alkanoyl side chains, polyoxy ethylene ether, phenoxy polyethoxy alcohol, phosphatidyl choline ester, phosphatidyl ether, tyloxapol, and $C_{22}H_{19}ClO_3$.

238. (New) The kit of claim 164, wherein the delivery device delivers single metered doses of a solid powdered or liquid aerosol or spray buccal, nasal, intracavitary, intraorgan or intrapulmonary formulation of the nucleic acid of particle size of about 0.5 μ to 10 μ or 10 μ to 500 μ.

239. (New) The kit of claim 164, wherein the delivery device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray; and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as an inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of the nucleic acid(s) of particle size about 0.5 μ to 10 μ or 10 μ to 500 μ.

240. (New) The kit of claim 164, wherein the delivery device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray, and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as a buccal, nasal, intracavitary, intraorgan, or intrapulmonary formulation of

particle size of about 0.5 μ to 10 μ or 10 μ to 500 μ of the nucleic acid.

241. (New) The kit of claim 164, wherein the delivery device comprises a pressurized device that delivers a solid powdered or liquid aerosol or spray of particle size 10μ to 500μ; and the nucleic acid is provided as an aerosolizable or sprayable suspension, solution, emulsion or dry powder formulation of particle size 10μ to 500μ.

242. (New) The kit of claim 164, wherein the nucleic acid is provided as a buccal, nasal, intracavitary, intraorgan, or intrapulmonary formulation of particle size 10μ to 500μ.

243. (New) The kit of claim 171, wherein the nucleic acid is provided as an inhalable, respirable, intracavitary, intraorgan or intrapulmonary formulation of particle size about 5μ to 10μ.

244. (New) The device of claim 222, wherein said device delivers a solid powdered or liquid aerosol or spray formulation of the nucleic acid of particle size about 0.5 μ to 10 μ.

245. (New) The device of claim 222, wherein said device delivers a solid powdered or liquid aerosol or spray formulation of the nucleic acid of particle size 10 μ to 500 μ.

246. (New) The device of claim 222, wherein said device delivers single metered doses of the formulation as a solid powdered or liquid aerosol or spray of the nucleic acid of particle size 10μ to 500μ.

247. (New) The device of claim 222, wherein the oligo(s) is anti-sense to the initiation codon, the coding region or the 5' or 3 ' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to increased levels of adenosine or an adenosine receptor, bronchoconsriction, asthma, lung allergy, or lung inflammation, or is anti-sense to the corresponding mRNA, and is effective in reducing hyper-responsiveness to adenosine, the amount of an adenosine receptor, or the production or availability of adenosine, or in increasing the degradation of an adenosine receptor or mRNA thereof.

248. (New) The method of claim 190, wherein the surfactant is selected from the group consisting of surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E, or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine,

dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinone, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate diacylglycerol, cytidine diphosphate choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acid, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene oxide block copolymers, non-ionic propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran side chains, poly (vinyl amine) with alkanoyl side chains, polyoxy ethylene ether, phenoxy polyethoxy alcohol, phosphatidyl choline ester, phosphatidyl ether, tyloxapol, a surfactant-associated protein and $C_{22}H_{19}ClO_3$.

249. (New) The method of claim 173, wherein the oligo comprises up to about 15%A.

250. (New) The method of claim 173, wherein the oligo(s) is (are) effective to alleviate hyper-responsiveness to adenosine or an adenosine receptor, reduce the level of adenosine, reduce the level of an adenosine receptor, or to alleviate bronchoconstriction, asthma, lung allergy or lung inflammation; wherein the oligo comprises up to and including about 15% adenosine, and is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to adenosine or an adenosine receptor, bronchoconstriction, asthma, lung allergy, or lung inflammation, or is anti-sense to the corresponding mRNA.

251. (New) The kit of claim 165, wherein the oligo(s) are effective to alleviate hyper-responsiveness to adenosine, to alleviate bronchoconstriction, asthma, lung allergy or lung inflammation, or to reduce the level of an adenosine receptor; wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene encoding a protein associated with hyper-responsiveness to adenosine or an adenosine receptor, bronchoconstriction, asthma, lung allergy or lung inflammation, or is anti-sense to the corresponding mRNA; wherein the nucleic acid comprises one or more oligo(s).

252. (New) The kit of claim 164, wherein the oligo(s) are effective to alleviate hyper-

responsiveness to increased levels of adenosine or adenosine receptors, or to alleviate bronchoconstriction, asthma, lung allergy, or lung inflammation, or to reduce levels of an adenosine receptor; wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene encoding a protein associated with hyper responsiveness to increased levels of adenosine or an adenosine receptor, or bronchoconstriction, asthma, lung allergy or lung inflammation, or being anti-sense to the corresponding mRNA; wherein the nucleic acid comprises one or more oligo(s); wherein the kit is suitable for the diagnosis or treatment of a disease or condition associated with hypersensitivity to increased levels of adenosine or an adenosine receptor, or bronchoconstriction, lung allergy, lung inflammation or asthma.

253. (New) The method of claim 173, further comprising administering a surfactant.

254. (New) The method of claim 253, wherein the surfactant is administered in a prophylactically or therapeutically effective amount.

255. (New) The aerosolizable or sprayable composition according to claim 108 wherein a surfactant is operatively linked to the nucleic acid.

256. (New) The aerosolizable or sprayable composition according to claim 108 wherein the adenosine receptor comprises an adenosine A_{2a} or A_{2b} receptor and the composition does not contain a surfactant.

257. (New) The composition of claim 117, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalhl, arylalkenyl, arylalkynyl, or arylcycloalkl is substituted by an O, halo, NH_2, primary, secondary or tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl.

258. (New) The composition of claim 208, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalhl, arylalkenyl, arylalkynyl, or

arylcycloalkl is substituted by an O, halo, NH_2, primary, secondary or tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl.

259. (New) The diagnostic or therapeutic kit of claim 164, further comprising an agent, wherein said agent is a therapeutic agent, diagnostic agent, anti-oxidant, filler, volatile oil, dispersant, flavoring agent, propellant, preservative, solvent, surfactant, buffering agent, RNA inactivating agent, agent that is internalized or up-taken by a cell, or coloring agent.--

REMARKS

Amendments

In the Amendment filed June 12, 2002, Applicant requested amendment of Claims 108, 115-117, 119, 124, 130-131, 135, 144, 146, 148, 152, 158-159, 162, 164-167, 170-171, 173, 179, 181, 183-187, 189, 191, 195, 200, 205, 207, 210, 219-227, 229, 232, to 234, and the addition of new Claims 235-254. Addition to the amendments requested in the Amendment filed June 12, 2002, Applicant now request the cancellation of Claim 168 and the further amendment of Claims 108-111, 113-127, 130-131, 135-137, 143-144, 146, 148, 151-153, 158-159, 161-162, 166, 169-171, 178-180, 184-187, 189, 193, 198, 201-203, 205-212, 214-216, 218-229, and 231-231; these amendments do not change the subject matter claimed and are made solely to clarify the subject matter claimed and to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants also request Examiner enter a further set of new claims: new Claims 255-259.

Claim 108 is amended to recite "aerosolizable or sprayable". Support for this amendment is found, for example, in page 46, lines 18-21 and page 51, lines 3-5.

Claims 109-111 and 201-203 are amended to recite "comprises". Support for this amendment is found, for example, in page 40, lines 23-26.

Claims 118 and 209 are amended to recite "purines are substituted at a . . 6 . . . position". Support for this amendment is found in page 41, lines 23-24, which teaches that "[t]he pyrimidines and purines may be substituted at **all** positions as is known in the art" (emphaiss added), and page 42, line 1, which depicts a generic pyrimidine and purine compound with position 6 labeled.

Claims 119 and 210 are amended to correctly spell the term "xanthine". The term was incorrectly spelled "xantine". These amendments are to correct obvious typographical errors.

Claim 124 is amended to delete the term "about" regarding the number of mononucleotides. Support is found, for example, in the claim as originally filed.

Claim 130 is amended to recite "comprises surfactant proteins, non-liposomal phospholipids, fatty acids, and surfactant-associated proteins, or mixtures thereof". Support for this amendment is found, for example, in page 44, line 17 to page 45, line 7.

Claim 131 is amended to replace "is selected from" with "comprises" in order to comply with the proper use of the Markush format. Support is found, for example, in the claim as originally filed.

Claim 131 is amended to recite "$C_{22}H_{19}ClO_3$ (Atovaquone®)". This amendments is to clarify that "$C_{22}H_{19}ClO_3$" is the correct chemical formula for Atovaquone®.

Claim 135 is amended to delete the term "gaseous". Support is found, for example, in the claim as originally filed.

Claim 144 is amended to recite "propellant". Support for this amendment is found, for example, in page 51, line 5.

Claim 152 are amended to recite the terms "sprayable" and "aerosolizable". Support for this amendment is found, for example, in page 46, lines 18-21 and page 51, lines 3-5.

Claim 164 is amended to recite "[a] diagnostic or therapeutic kit for delivery of an oligonucleotide(s) (oligo(s))". Support for this amendment is found, for example, in Claim 57 as originally filed.

Claims 164, 166, 167, 170, 173, and 222 are amended to recite "non-liposomal". The present claimed agents is hydrophilic and support is found, for example, in page 45, line 17, which teaches "sterile pyrogen-free saline solution" as a "suitable pharmaceutical acceptable carrier". Further, support for this amendment is found, for example, in page 46 lines 21-22, which teaches that '[t]he formulation of the invention **may** also comprise . . . a liposome". This teaching means that formulation of the invention is otherwise "non-liposomal".

Claims 164 and 222 are amended to recite "about 0.5 μ to 500 μ". Support for this amendment is found, for example, in page 48, lines 24-27.

Claims 165-167, 171, 173, 183, and 223-225 are amended to recite "10 μ to 500 μ". Support for this amendment is found, for example, in page 48, line 27.

Claim 165 is amended to recite "inhalable, respirable, intracavitray, intraorgan or intrapulmonary". Support for this amendment is found, for example, in Claim 167 as originally filed.

Claim 179 is amended to recite "anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene encoding a protein associated with hyper-responsivesness to adenosine, increased levels of adenosine, increased levels of an adenosine receptor, broncoconstriction, asthma, lung allergy or lung inflammation, or is anti-sense to the corresponding mRNA". Support for this amendment is found, for example, in page 44, lines 2-9.

Claims 181 and 183 are amended to depend from Claim 173. Support for this amendment is found in Claim 181 (which originally depended from Claim 178, which in turn depended from Claim 173) and Claim 183 181 (which originally depended from Claim 181, which in turn depended from Claim 173).

Claim 184 is amended to recite "further comprising administering a surfactant, which may be in the same composition as the nucleic acid". Support for this amendment is found, for example, in page 4, lines 6-8.

Claim 185 is amended to depend from Claim 179. Support for this amendment is found in original Claim 185 (which originally depended from Claim 173, from which Claim 179 depends).

Claims 185-187, and 221 are amended to recite "increased levels of adenosone (A) receptors, and/or". Support for this amendment is found, for example, in page 10, lines 17-20.

Claim 186 is amended to recite "allergies". Support for this amendment is found, for example, in page 4, line 16.

Claim 191 is amended to recite "a surfactant protein, non-liposomal phospholipid, fatty acid, or surfactant-associated protein". Support for this amendment is found, for example, in page 44, line 17 to page 45, line 7. Applicants clarify that in the Response filed June 12, 2002, in the clean version of the amended claims, Claim 191 was inadvertently labeled Claim 190. In this Response, Applicant amends Claim 191 in order to further clarify the subject matter claimed.

Claim 195 is amended to insert an "an" in order to correct an obvious typographic error.

Claims 200, 206, and 219 are amended in order that these claims depend from Claim 179 instead of Claim 173.

Claim 207 is amended to insert an "or" in order to correct an obvious typographic error.

Claim 212 is amended to recite "wherein said oligonucleotide comprises a methylated cytosine". Support for this amendment is found, for example, in Claim 101 as originally filed.

Claim 220 is amended to recite "comprise" instead of "is selected from" in order that this claims be in a proper Markush format.

Claim 222 is amended to recite "their mixtures, or their pharmaceutically or veterinarily acceptable salts". Support for this amendment is found, for example, in page 4, line 12, page 44, line 15, and Examples 3 (page 54) and 5 (page 58), which show its veterinary use.

Claims 225-227 are amended to recite "device" instead of "inhaler". Support for this amendment is found, for example, in page 50, line 22.

Further, regarding the amendments requested in this Response, Claims 108-111, 113-127, 130-131, 135-137, 143-144, 146, 148, 151-153, 158-159, 161-162, 166, 169-171, 178-180, 184-187, 189, 193, 198, 201-203, 205-212, 214-216, 218-229, and 231-231 were amended to delete the terms "and/or", "may" and/or "if", to correct typographic errors, to make claims grammatical, and/or to place claims in a proper Markush format.

Support for new Claims 235 and 249 are found, for example, in page 40, lines 23-25.

Support for new Claims 236, 237, and 248 are found, for example, in page 44, line 12 to page 45, line 7.

Support for new Claims 238-246 are found, for example, in page 46, line 22, page 48, lines 24-27, page 50, lines 2-22, and Claim 79 as originally filed

Support for new Claims 247 and 250-252 are found, for example, in page 4, lines 15-17, page 9, lines 8-14, page 40, lines 23-25, and page 44, lines 2-9.

Support for new Claim 253 is found, for example, in page 4, line 7.

Support for new Claim 254 is found, for example, in page 5, lines 6-7.

Support for new Claim 255 is found, for example, in page 4, line 7.

Support for new Claim 256 is found, for example, in page 12, line 19, and in page 43, lines 25-26 which teaches that the "antisense nucleotides may be administered in the form of their pharmaceutically acceptable salts or as a mixture" wherein no surfactant is taught to be

included in this formulation.

Support for new Claim 257 is found in original Claim 10 as filed.

Support for new Claim 258 is found in original Claim 10 as filed.

Support for new Claim 259 is found in original Claim 29 as filed.

Applicant's have enclosed a complete set of the claims and amended claims in the condition desired after taking into account the above amendments. Also enclosed is a complete set of claim and amended claims showing the changes made by the above amendments.

Applicant reserves the right to reintroduce the original claims in one or more continuation type of application. Applicant respectfully contends that the amendments will place the case in condition for allowance. No new matter is added in any of the above amendments and the Examiner is respectfully requested to enter the amendments and reconsider the application.

Remarks

Claims 108-132, 134-141, 143-144, 146, 148, 151-153, 158-159, 161-163, 164-167, 169-173, 178-181, 184-189, 191-193, 195-198, and 200-234 are pending in the present application. In addition, Applicant requests Examiner enter new Claims 235-259. Claim 168 is cancelled.

1. 35 U.S.C. 112, second paragraph.

The Examiner's rejection of Claim 191 under 35 U.S.C. §112, second paragraph should be withdrawn, because Claim 191 as amended recites a Markush group with proper use of the Markush format.

The Examiner rejects Claim 191 under 35 U.S.C. 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner alleges that Claim 191 appears to claim a Markush group without proper use of the Markush format. Claim 191 as amended recites "a surfactant protein, non-liposomal phospholipid, fatty acid or surfactant-associated protein". Claim 191 as amended recites a Markush group with proper use of the Markush format.

Since amended Claim 191 is clear and definite, this rejection should be withdrawn.

2. 35 U.S.C. 112, first paragraph.

The Examiner's rejection of Claim 222 under 35 U.S.C. §112, first paragraph for lack of written description should be withdrawn, because Claim 222 as amended recites "about 0.5 to 500 μ".

The Examiner rejects Claim 222 under 35 U.S.C. 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner alleges that "neither the specification as filed, nor the original claims provide support for the limitations wherein the '. . . particle size about 0.5 μ to about 500 μ'". The Applicant traverse this rejection in that the specification teaches that: "In general, respirable particles range from **about .5 to 10 microns** in size. . . . For nasal administration, a particle size in the range of **10-500 μm** is preferred to ensure retention in the nasal cavity." (page 48, line 23 to page 49, line 1; emphasis added). These two ranges of particle size teach a continuous range of particle size from "about 0.5 μ" to "500 μ", since the two ranges taught overlap at 10 μ. The unit of measure "μ" is equal to "micron" and "μm" (micrometer). and the length of 1 micrometer is equal to 10^{-6} m.

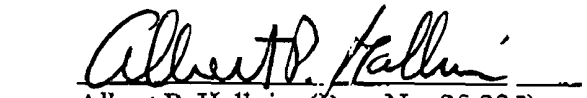
Since the subject matter of Claim 222 is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, therefore this rejection of Claim 222 should be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, the Applicant believes that the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 463-8109.

Respectfully submitted,

Date: December 20, 2002



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